

Applicant(s): Neil Bander
METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
INSULIN-RELATED DISORDERS USING BINDING AGENTS
SPECIFIC FOR PROSTATE SPECIFIC MEMBRANE ANTIGEN

Amino Acid Sequence of Murine J591 Heavy Chain (CDRs are marked
numbering as Kabat)

EVQLQQSGPELKKPGTSVRISCKTS | GYTFTEYTIH | WVKQSHGKS
1 10 20 30 40
CDR1

LEWIG | NINPNNGGTTYNQKFED | KATLTVDKSSSTAYMELRSLTS
50 60 70 80
CDR2

EDSAVYYCAA | GWNFDY | WGQGTTLTVSS
90 100 110
CDR3

FIG. 1A

Amino Acid Sequence of Murine J591 Light Chain (CDRs are marked
numbering as Kabat)

DIVMTQSHKFMSTSVGDRVSIIC | KASQDVGTAVD | WYQQKPGQSP
1 10 20 30 40
CDR1

KLLIY | WASTRHT | GVPDRFTGSGSGTDFTLTITNVQSEDLADYFC
50 60 70 80
CDR2

| QQYNSYPLT | FGAGTMLDLK
90 100
CDR3

FIG. 1B

Amino Acid Sequence of DeImmunised J591 Heavy Chain (CDRs are marked, numbering as Kabat)

EVQLVQSGPEVKKPGATVKISCKTS|GYTFTEYTIH|WVKQAPGKG
1 10 20 30 40
CDR1

LEWIG|NINPNNGGTTYNQKFED|KATLTVDKSTDTAYMELSSLRS
50 60 70 80
CDR2

EDTAVYYCAA | GWNFDY | WGQGTLLTVSS
90 100 110
CDR3

FIG. 2A

Amino Acid Sequence of DeImmunised J591 Light Chain (CDRs are marked, numbering as Kabat)

DIQMTQSPSSLSTSVGDRVTLTC | KASQDVGTAVD | WYQQKPGSP
1 10 20 30 40
CDR1

KLLIY|WASTRHT|GIPSRFSGSGSGTDFTLTISLQPEDFADYYC
 50 60 70 80
 CDR2

90 100
CDR3

FIG. 2B

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Location of T cell epitopes in J591 VH

	10	20		
1	E V Q L Q Q S G P E L V K P G T S V R I S C K T S		J591 MoVH	
1	E V Q L V Q S G P E V K K P G A T V K I S C K T S		J591 DIVH	
	30	40	50	
26	G Y T F T E Y T I H W V K Q S H G K S L E W I G N		J591 MoVH	
26	G Y T F T E Y T I H W V K Q A P G K G L E W I G N		J591 DIVH	
	60	70		
51	I N P N N G G T T Y N Q K F E D K A T L T V D K S		J591 MoVH	
51	I N P N N G G T T Y N Q K F E D K A T L T V D K S		J591 DIVH	
	80	90	100	
76	S S T A Y M E L R S L T S E D S A V Y Y C A A G W		J591 MoVH	
76	T D T A Y M E L S S L R S E D T A V Y Y C A A G W		J591 DIVH	
	110			
101	N F D Y W G Q G T T L T V S S		J591 MoVH	
101	N F D Y W G Q G T L L T V S S		J591 DIVH	

FIG. 3A

Location of T cell epitopes in J591 VK

10										20																			
1	D	I	V	M	T	Q	S	H	K	F	M	S	T	S	V	G	D	R	V	S	I	I	C	K	A	J591 MoVK			
1	D	I	Q	M	T	Q	S	P	S	S	L	S	T	S	V	G	D	R	V	T	L	T	C	K	A	J591 DIVK			
30										40										50									
26	S	Q	D	V	G	T	A	V	D	W	Y	Q	Q	K	P	G	Q	S	P	K	L	L	I	Y	W	J591 MoVK			
26	S	Q	D	V	G	T	A	V	D	W	Y	Q	Q	K	P	G	P	S	P	K	L	L	I	Y	W	J591 DIVK			
60										70										80									
51	A	S	T	R	H	T	G	V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I	J591 MoVK			
51	A	S	T	R	H	T	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	J591 DIVK			
90										100										110									
76	T	N	V	Q	S	E	D	L	A	D	Y	F	C	Q	Q	Y	N	S	Y	P	L	T	F	G	A	J591 MoVK			
76	S	S	L	Q	P	E	D	F	A	D	Y	Y	C	Q	Q	Y	N	S	Y	P	L	T	F	G	P	J591 DIVK			
120										130										140									
101	G	T	M	L	D	L	K																			J591 MoVK			
101	G	T	K	V	D	I	K																			J591 DIVK			

FIG. 3B

FIG. 3B

J591 MoVK
 J591 DIVK

J591 MoVK
 J591 DIVK

J591 MoVK
 J591 DIVK

J591 MoVK
 J591 DIVK

J591 MoVK
 J591 DIVK

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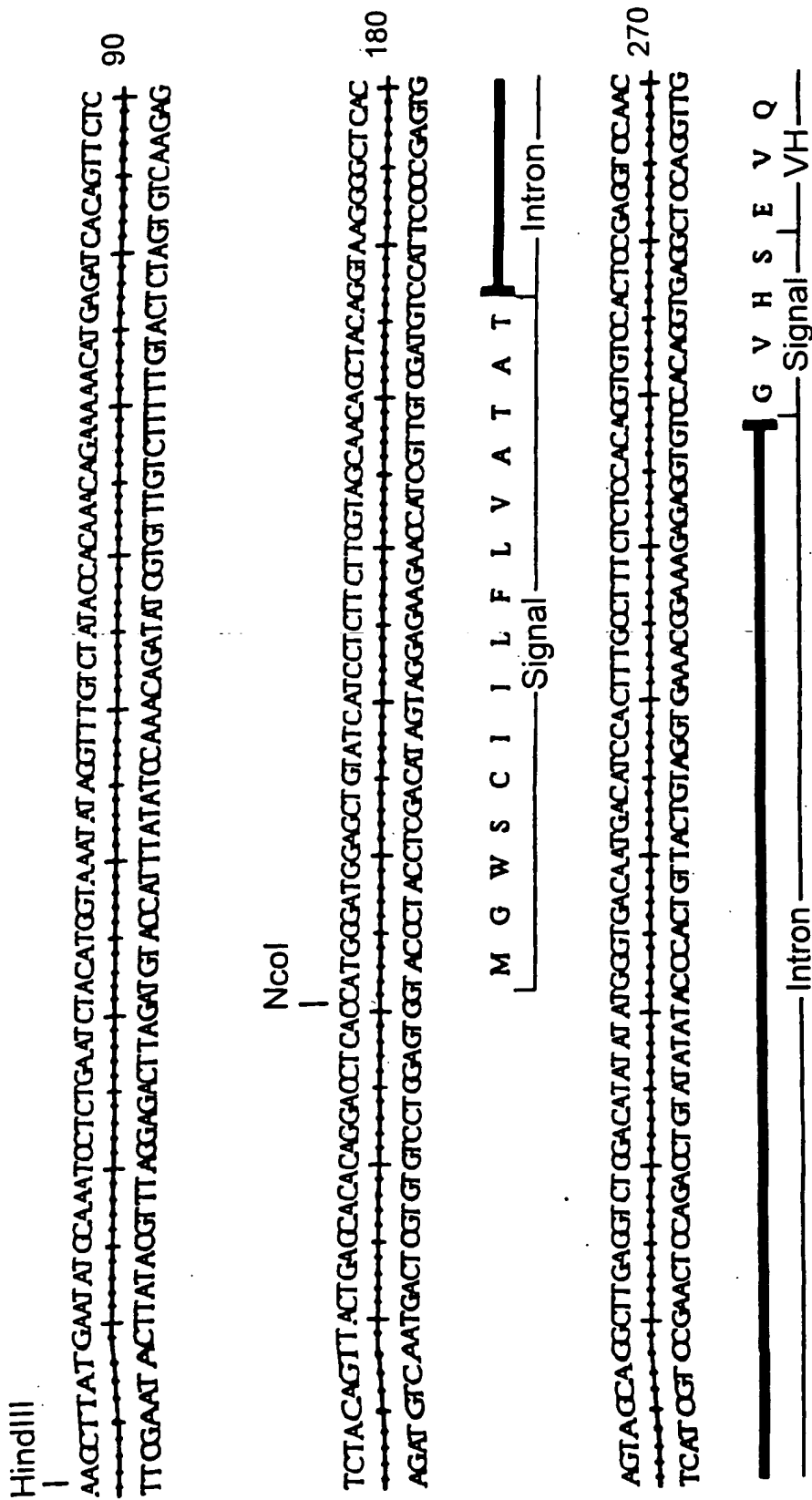
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FIG. 4A-1

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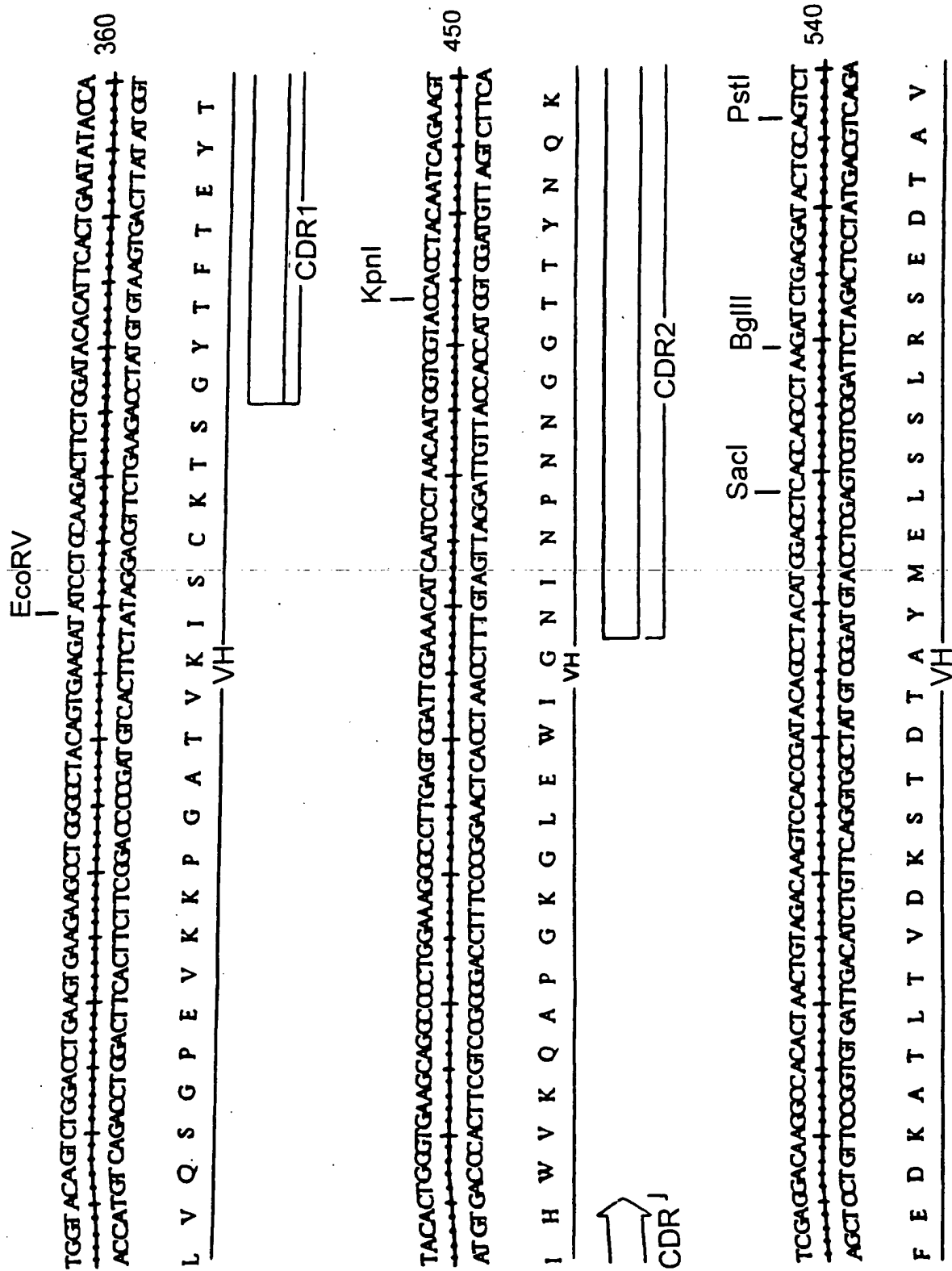
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FIG. 4A-2

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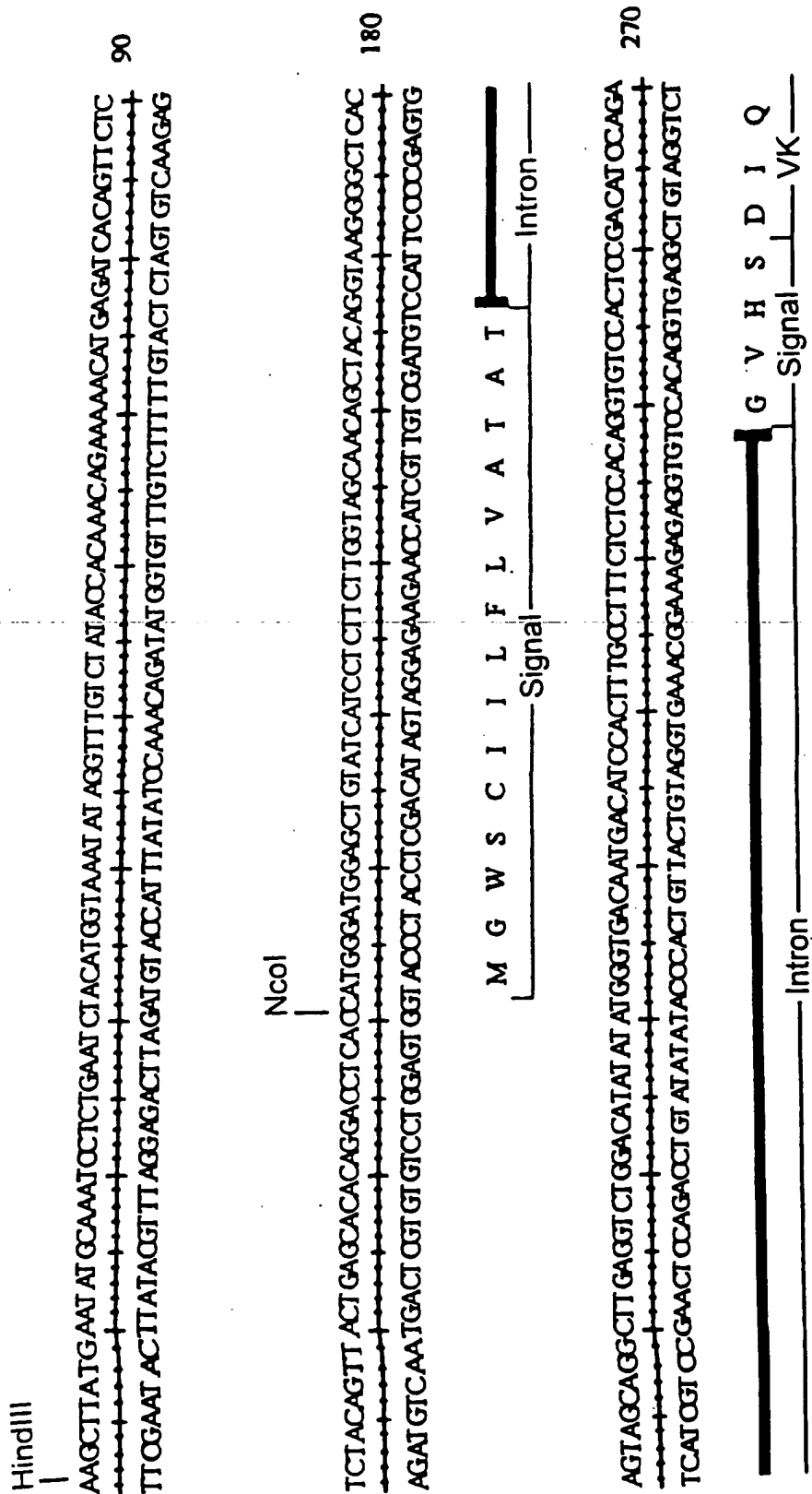
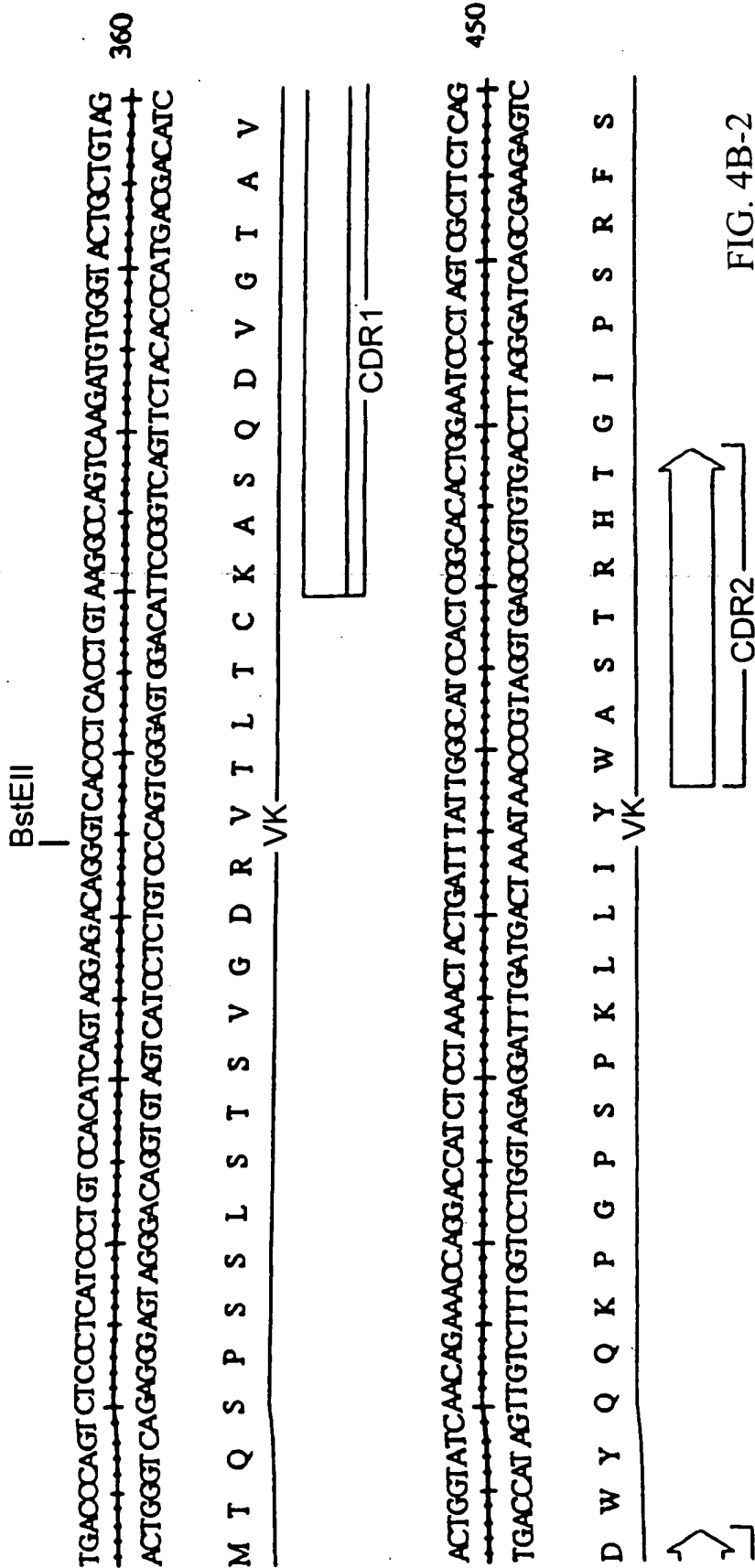
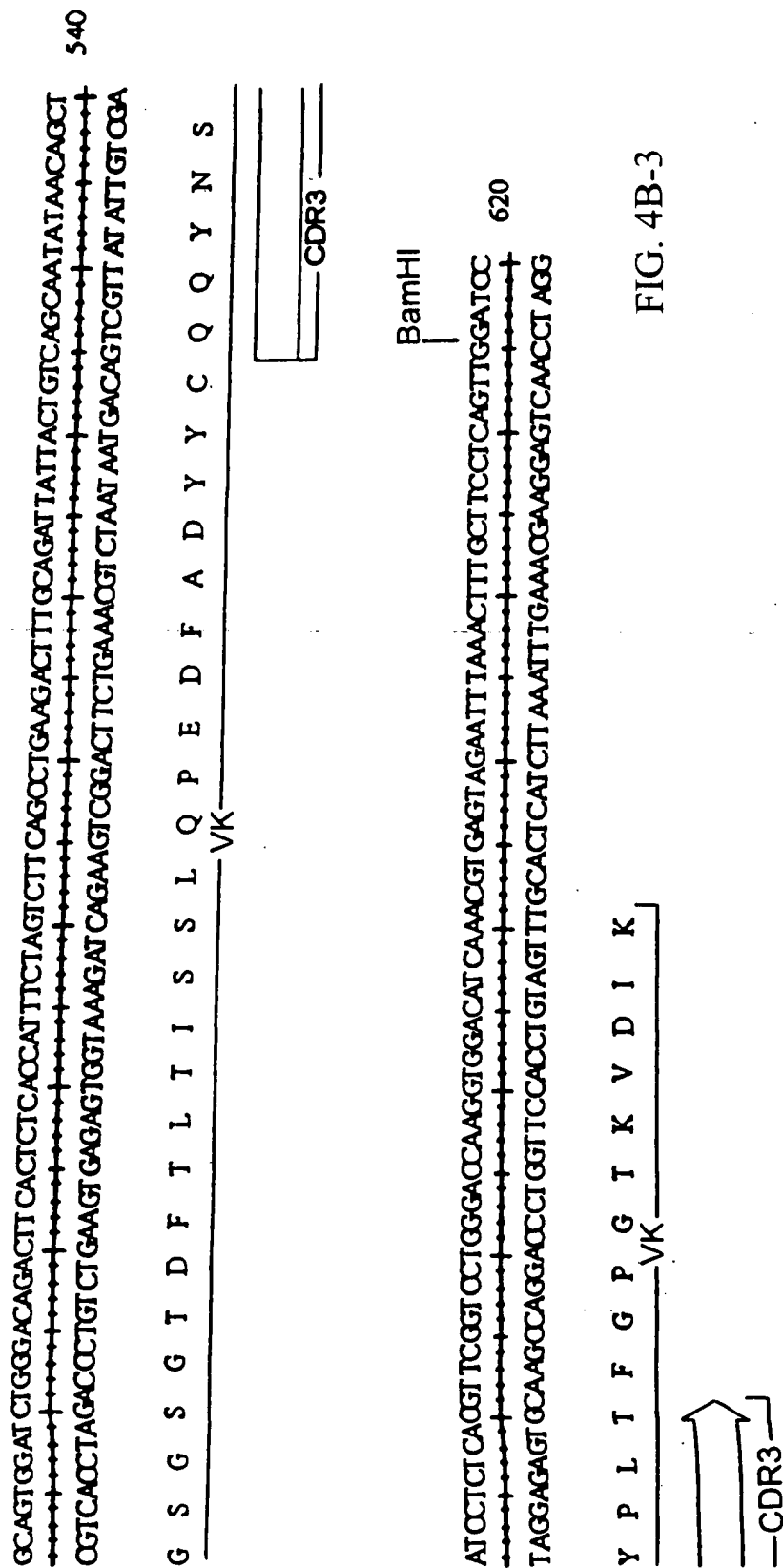
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FIG. 4B-I

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E V K L E E S G G G L V Q P G G S M K I S C V A S G F T F										Majority
10 20										
1	E	V	K	L	E	E	S	G	G	J415VH
1	E	V	K	L	E	E	S	G	G	J415DIVH1
1	E	V	K	L	E	E	S	G	G	J415DIVH2
1	E	V	K	L	E	E	S	G	G	J415DIVH3
1	E	V	K	L	E	E	S	G	G	J415DIVH4
S N Y W M N W V R Q T P E K G L E W V A E I R S Q S N N F										Majority
30 40 50										
30	S	N	Y	W	M	N	W	V	R	J415VH
30	S	N	Y	W	M	N	W	V	R	J415DIVH1
30	S	N	Y	W	M	N	W	V	R	J415DIVH2
30	S	N	Y	W	M	N	W	V	R	J415DIVH3
30	S	N	Y	W	M	N	W	V	R	J415DIVH4
A T H Y A E S V K G R V I I S R D D S K S S V Y L Q M N S										Majority
60 70 80										
59	A	T	H	Y	A	E	S	V	K	J415VH
59	A	T	H	Y	A	E	S	V	K	J415DIVH1
59	A	T	H	Y	A	E	S	V	K	J415DIVH2
59	A	T	H	Y	A	E	S	V	K	J415DIVH3
59	A	T	H	Y	A	E	S	V	K	J415DIVH4
L R A E D T A V Y Y C T R R R W N N F W G Q G T T V T V S S										Majority
90 100 110										
88	L	R	A	E	D	T	A	V	Y	J415VH
88	L	R	A	E	D	T	A	V	Y	J415DIVH1
88	L	R	A	E	D	T	A	V	Y	J415DIVH2
88	L	R	A	E	D	T	A	V	Y	J415DIVH3
88	L	R	A	E	D	T	A	V	Y	J415DIVH4

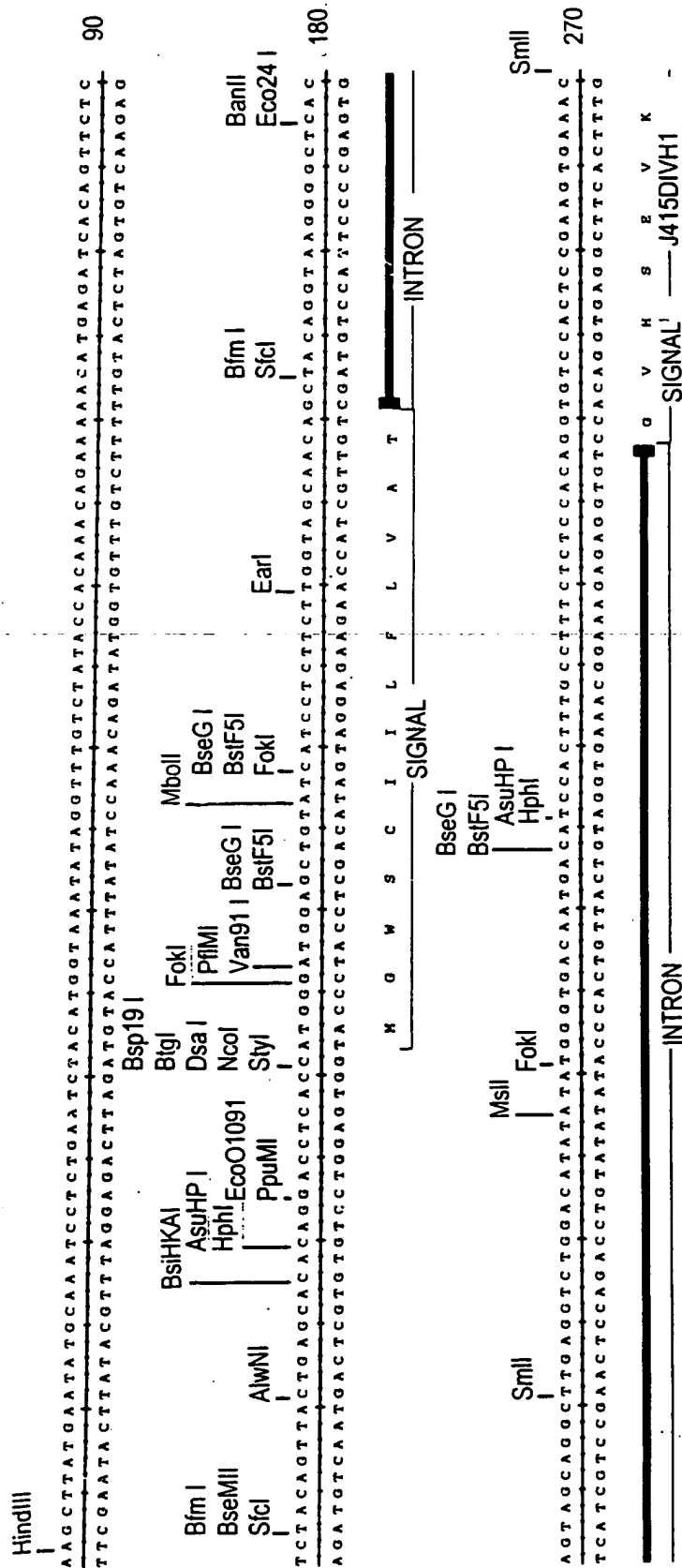
FIG. 5

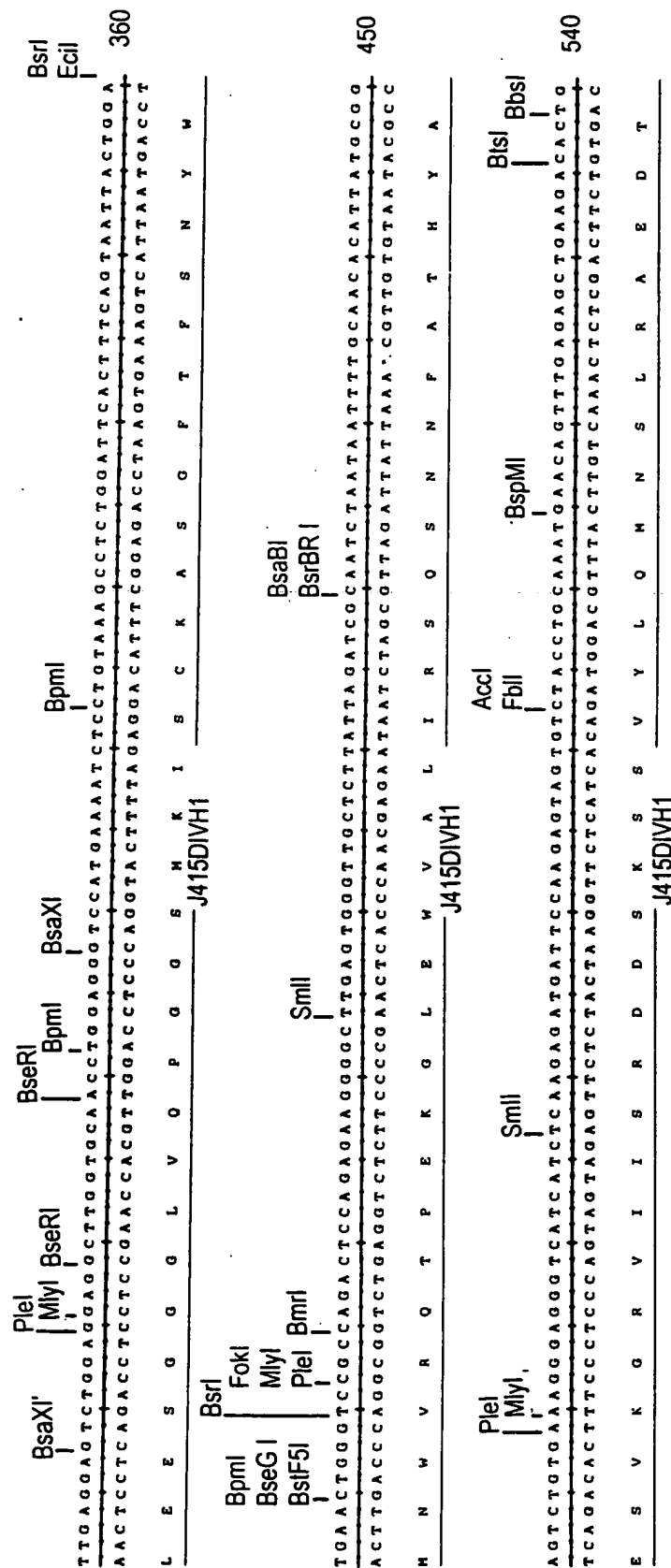
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N I V M T Q F P K S M S A S A G E R M T L T C K A S E																									Majority									
10										20																								
1	N	I	V	M	T	Q	F	P	K	S	M	S	I	S	V	G	E	R	V	T	L	T	C	K	A	S	E	J415VK						
1	N	I	V	M	T	Q	S	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK1						
1	N	I	V	M	T	Q	S	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK2						
1	N	I	V	M	T	Q	S	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK3						
1	N	I	V	M	T	Q	S	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK4						
1	N	I	V	M	T	Q	F	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK5						
1	N	I	V	M	T	Q	F	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK6						
1	N	I	V	M	T	Q	F	P	K	S	M	S	A	S	A	G	E	R	V	T	L	T	C	K	A	S	E	J415DIVK7						
1	N	I	V	M	T	Q	F	P	K	S	M	S	A	S	A	G	E	R	M	T	L	T	C	K	A	S	E	J415DIVK8						
N V G T Y V S W Y Q Q K P T Q S P K M L I Y G A S N R																									Majority									
30										40										50														
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	E	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415VK						
28	N	S	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK1						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK2						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK3						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK4						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK5						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	E	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK6						
28	N	V	G	T	Y	V	S	W	Y	Q	Q	K	P	T	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK7						
28	N	S	G	T	Y	V	S	W	Y	Q	Q	K	P	E	Q	S	P	K	M	L	I	Y	G	A	S	N	R	J415DIVK8						
F T G V P D R F S G S G S G T D F I L T I S S V Q A E																									Majority									
60										70										80														
55	F	T	G	V	P	D	R	F	T	G	S	G	S	A	T	D	F	I	L	T	I	S	S	V	Q	T	E	J415VK						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	A	S	S	V	Q	A	E	J415DIVK1						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	A	S	S	V	Q	A	E	J415DIVK2						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	A	S	S	V	Q	A	E	J415DIVK3						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	I	S	S	V	Q	A	E	J415DIVK4						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	I	S	S	V	Q	A	E	J415DIVK5						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	I	S	S	V	Q	A	E	J415DIVK6						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	I	S	S	V	Q	A	E	J415DIVK7						
55	F	T	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	I	L	T	I	S	S	V	Q	A	E	J415DIVK8						
D L V D Y Y C G Q S Y T F P Y T F G G G T K L E M K																									Majority									
90										100																								
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415VK							
82	D	P	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK1							
82	D	P	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK2							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK3							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK4							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK5							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK6							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK7							
82	D	L	V	D	Y	Y	C	G	Q	S	Y	T	F	P	Y	T	F	G	G	G	T	K	L	E	M	K	J415DIVK8							

FIG. 6





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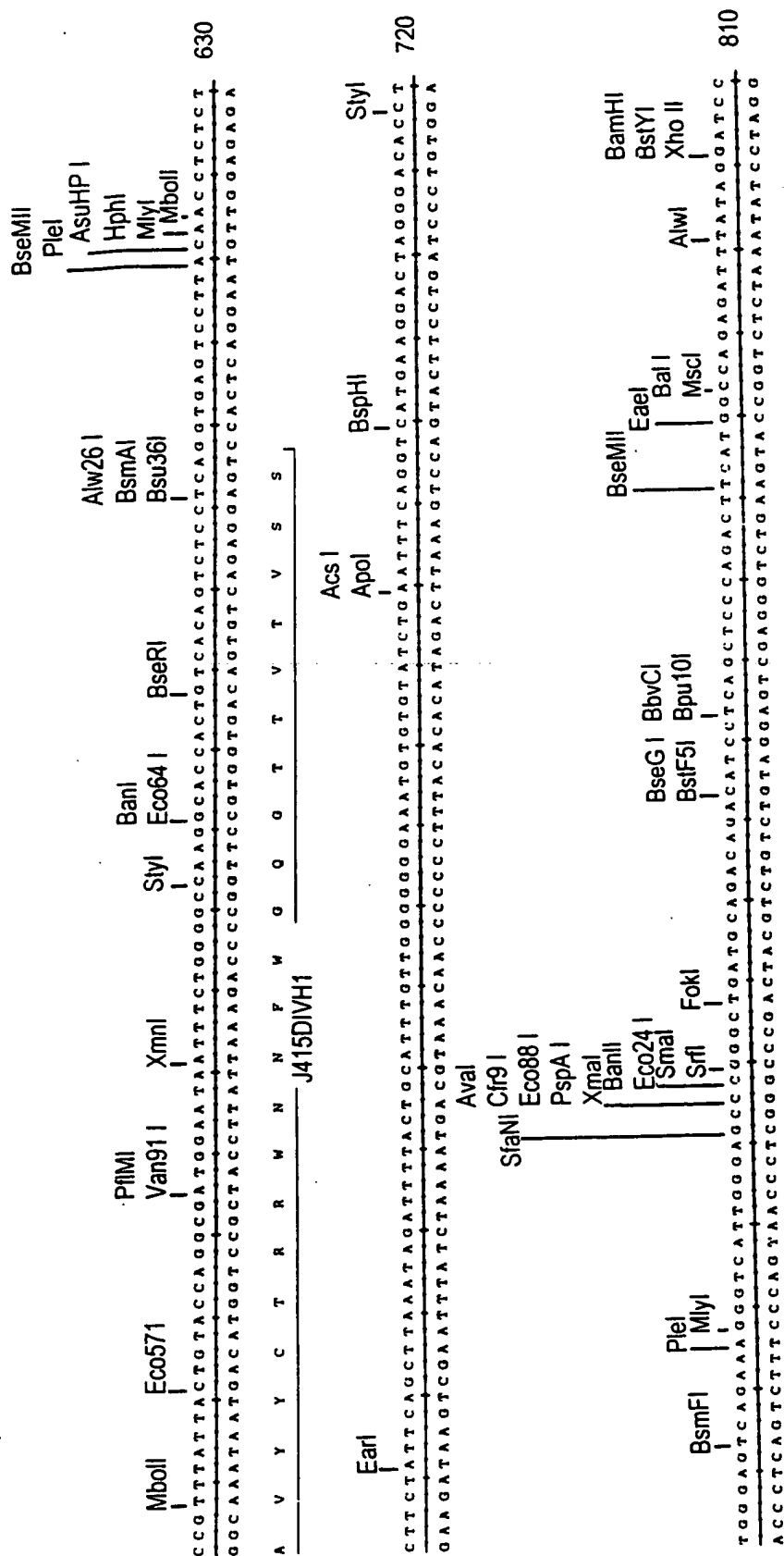
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FIG. 7A-3

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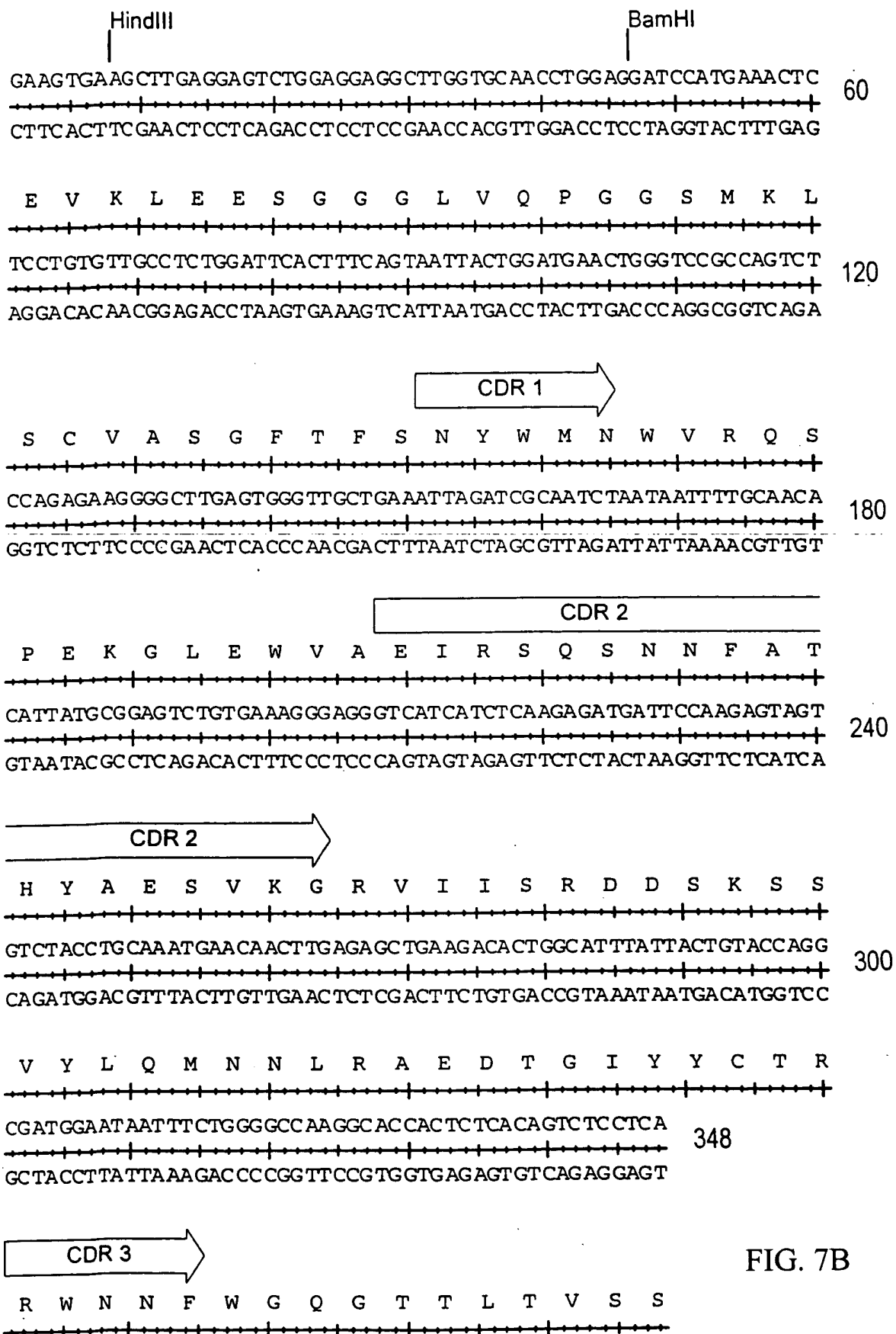
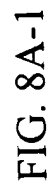
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FIG. 7B

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	E V K L E E S G G G L V Q P G G S M K L S C V A S G F T F S	Majority
	10 20 30	
1	E V K L E E S G G G L V Q P G G S M K L S C V A S G F T F S	J415vh
1	E V K L E E S G G G L V Q P G G S M K L S C V A S G F T F S	MUVHIIIIO
	N Y W M N W V R Q S P E K G L E W V A E I R L Q S D N F A T	Majority
	40 50 60	
31	N Y W M N W V R Q S P E K G L E W V A E I R S Q S N N F A T	J415vh
31	N Y W M N W V R Q S P E K G L E W V A E I R L K S D N Y A T	MUVHIIIIO
	H Y A E S V K G R V I I S R D D S K S S V Y L Q M N N L R A	Majority
	70 80 90	
61	H Y A E S V K G R V I I S R D D S K S S V Y L Q M N N L R A	J415vh
61	H Y A E S V K G R F T I S R D D S K S S V Y L Q M N N L R A	MUVHIIIIO
	E D T G I Y Y C T T G G Y G G R R S W N A F W G Q G T L V T	Majority
	100 110 120	
91	E D T G I Y Y C T - - - - - R R W N N F W G Q G T T L T	J415vh
91	E D T G I Y Y C T T G G Y G G R R S W F A Y W G Q G T L V T	MUVHIIIIO
	<u>V S S</u>	Majority
114	<u>V S S</u>	J415vh
121	<u>V S S</u>	MUVHIIIIO

FIG. 7C



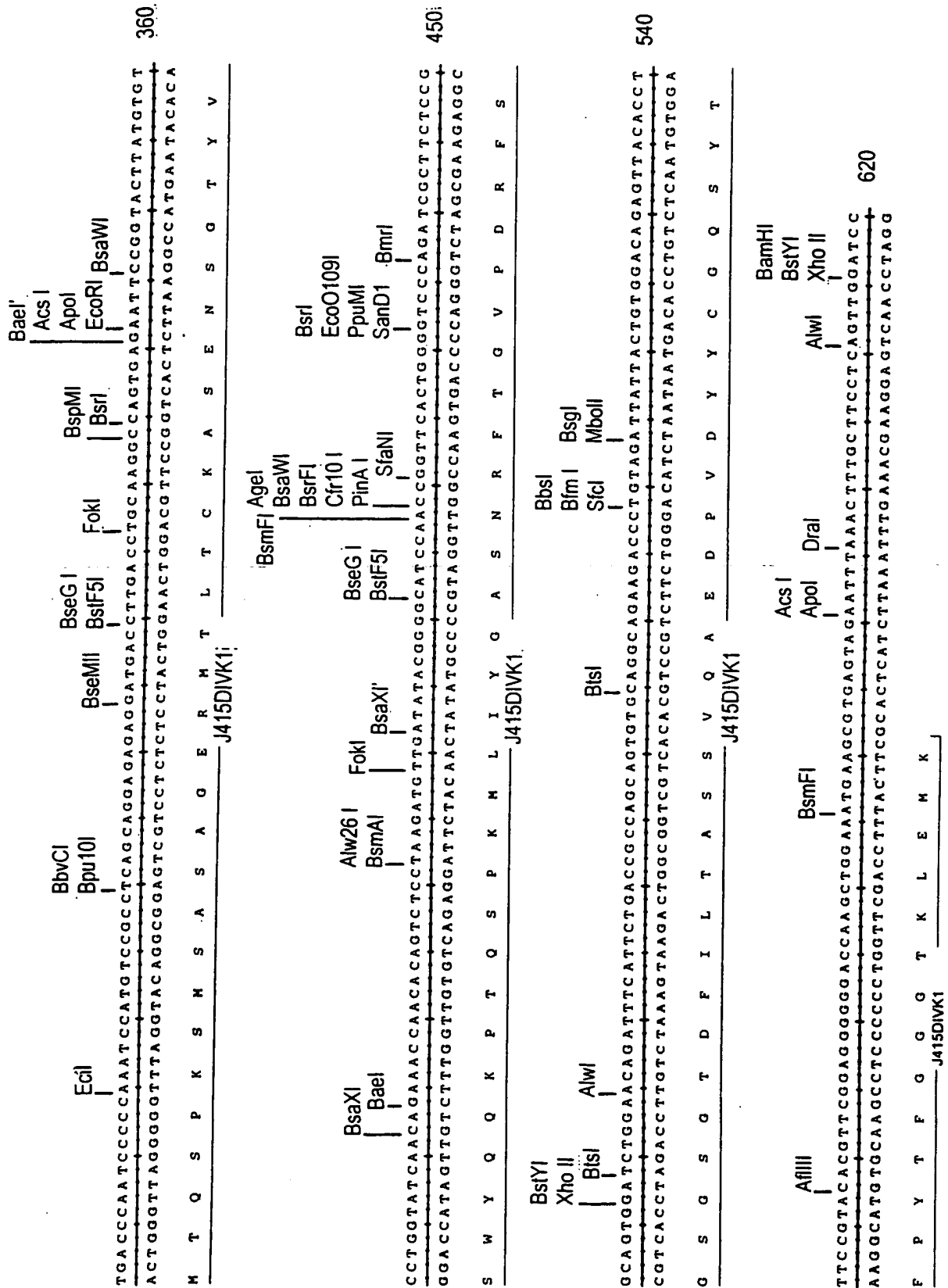


FIG. 8A-2

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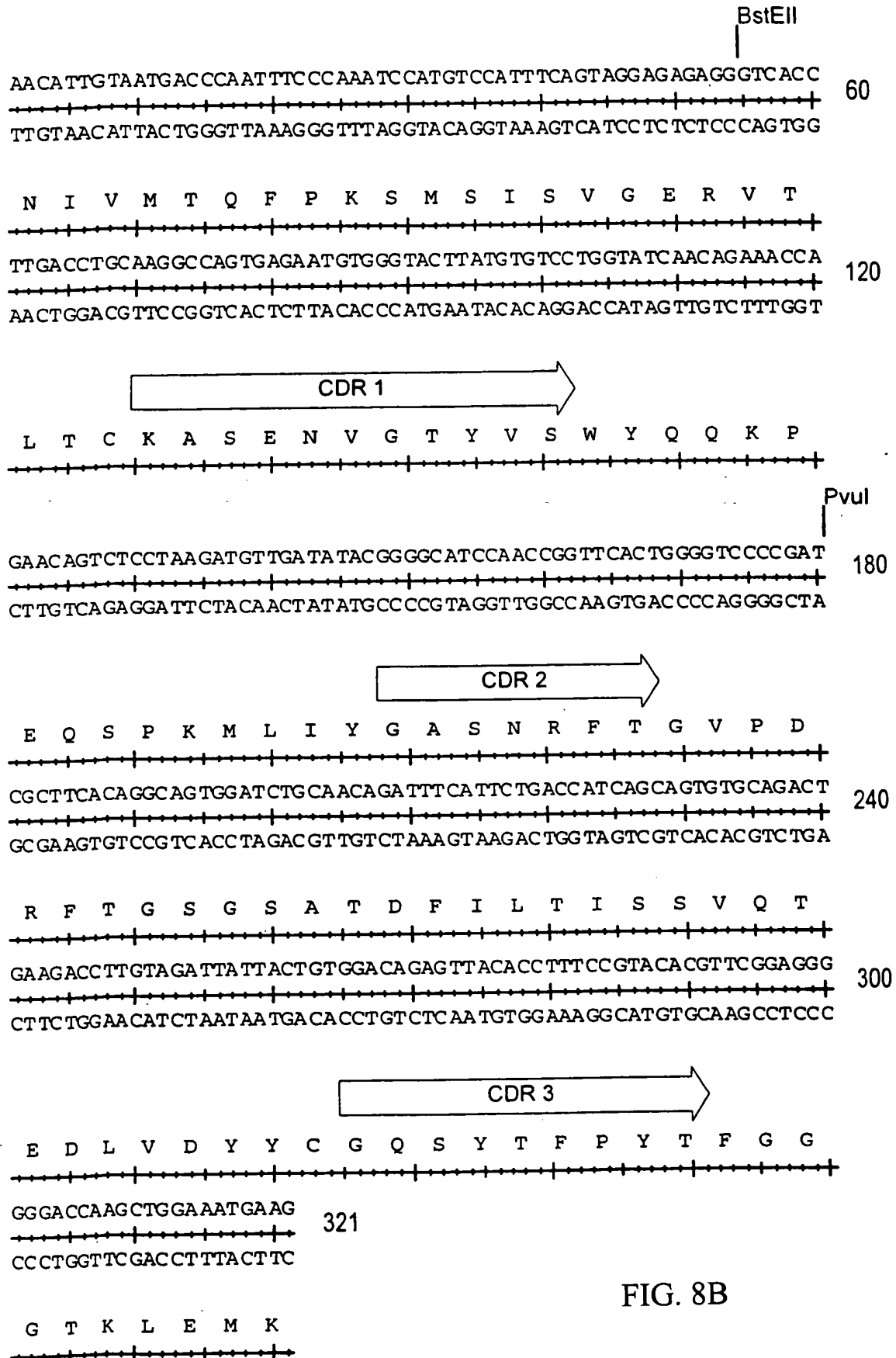
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FIG. 8B

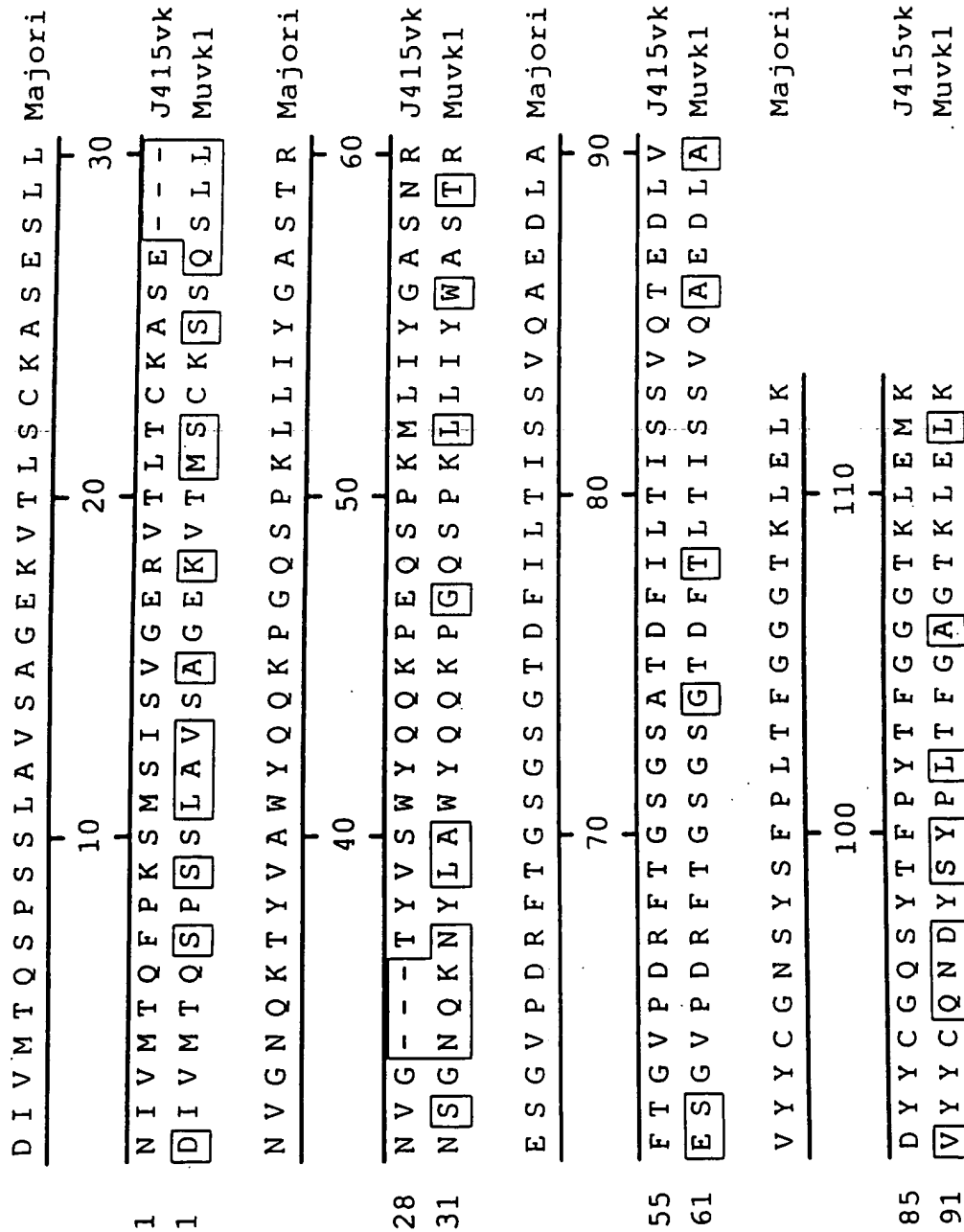


FIG. 8C

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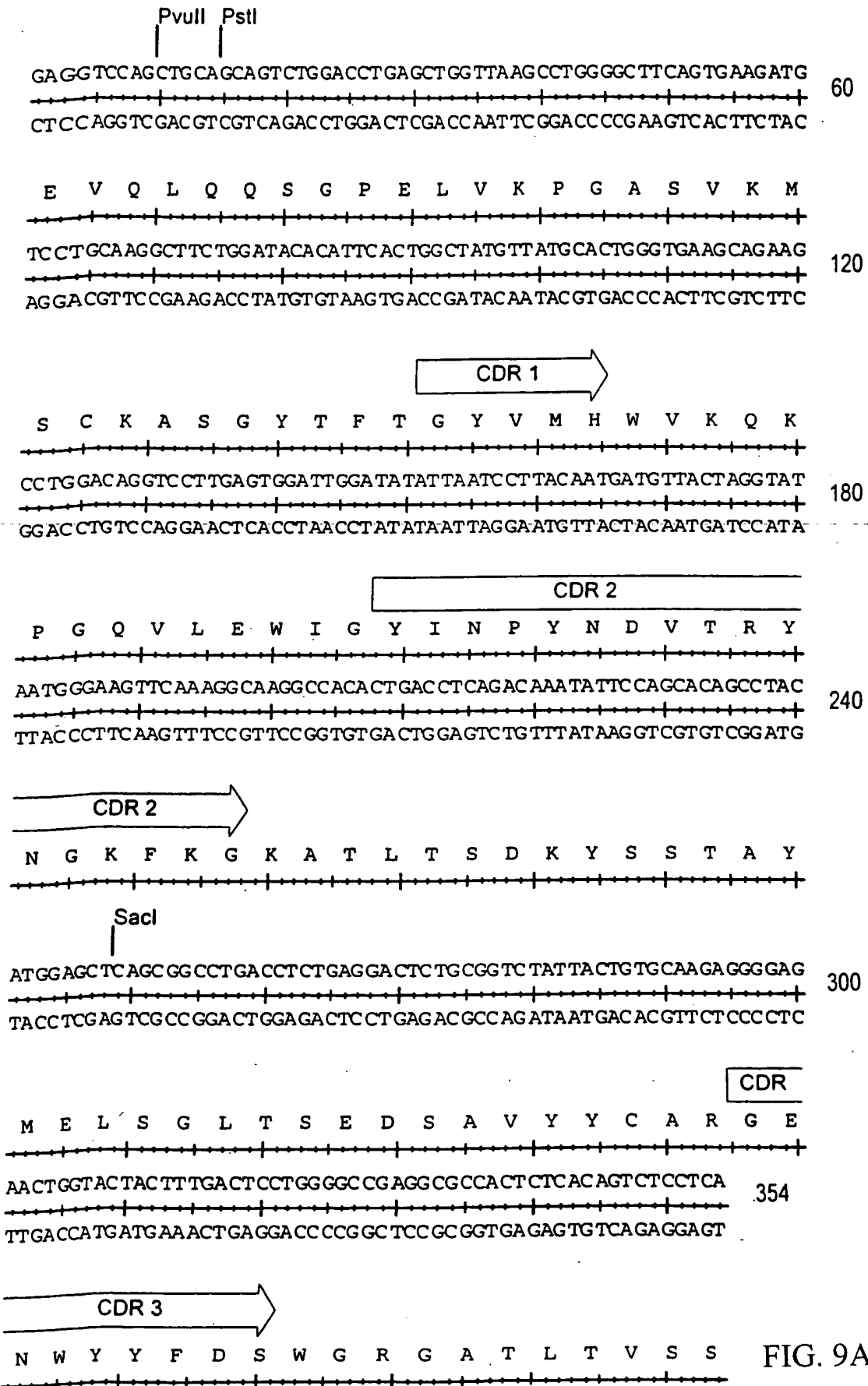
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FIG. 9A

Applicant(s): Neil Bander

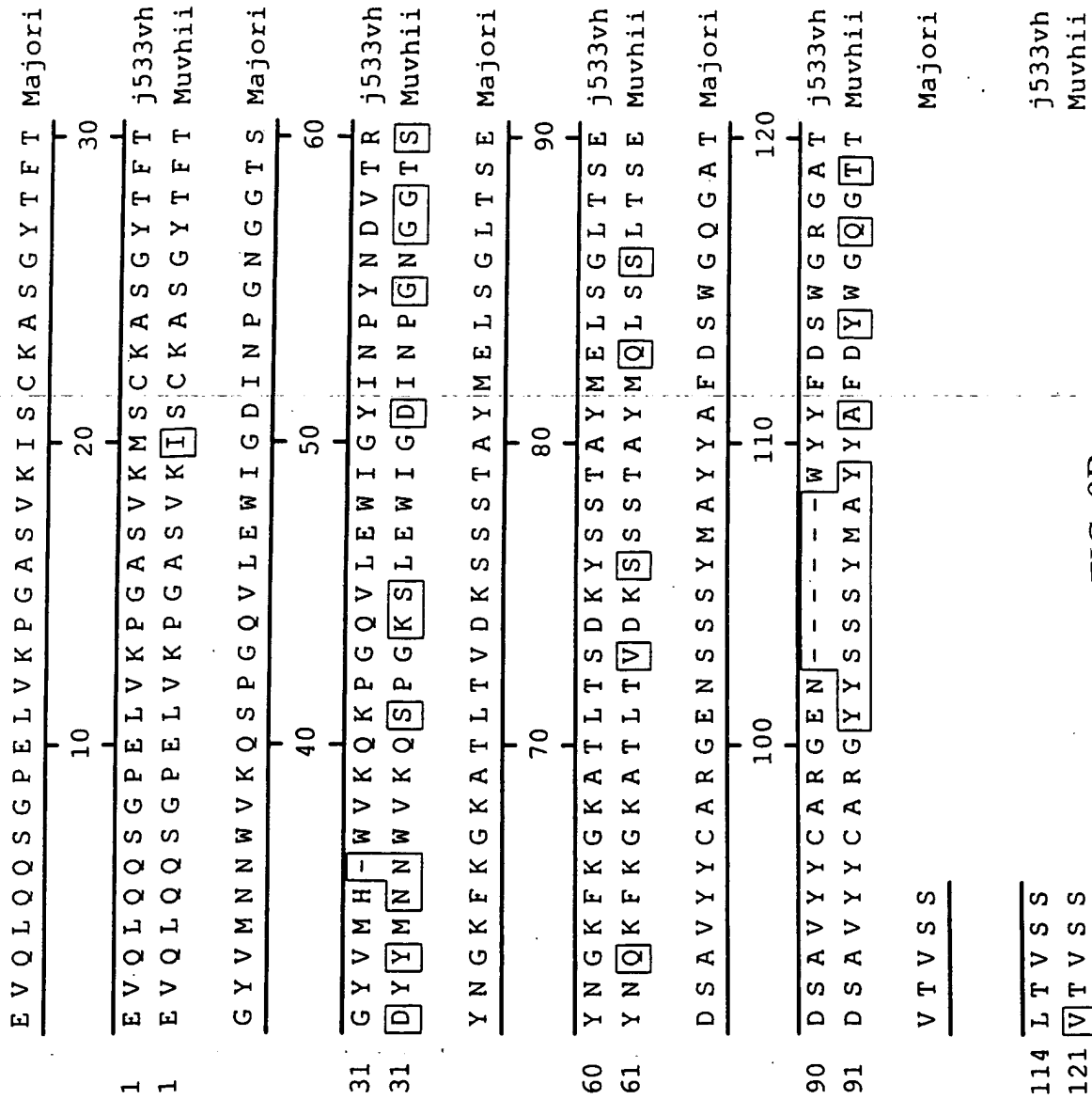
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FIG. 9B

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GACA TTG TGT GAC CCA ATCTC CAG CTTC TTTGG CTG TGTCT TAGGAC AGAGGGCC ACC
CTGT AAC AC GAC TGGGT TAGAGGT CGAAGAA CC GAC ACAGAGATCC TGTCTCC CGGTGG

D I V L T Q S P A S L A V S L G Q R A T

PstI

KpnI

ATATCCTGCAGAGCCAGTGAAAGTATTGATAGTTATGACAATACTTTATGCACTGGTAC
TATAGGACGTCTCGGTCACTTTCATAACTATCAATACGTATTATGAAAATACGTGACCATG

120

CDR 1

I S C R A S E S I D S Y D N T F M H W Y
CAGCAGAAACAGGACAGCCACCCAACTCCTCATCTTTCGTGCATCCATCC TAGAATCT
GTCGTCTTTGGTCCGTGCGGTGGTTGGAGGAGTAGAAAGCA CGTAGGTAGGATCTTAGA

180

CDR 2

Q Q K P G Q P P N L L I F R A S I L E S

BamHI

GGGATCCCTGCCAGGTTCA GTGGC AGTGGGTC TGGGA CAGACTTCAC CCTCACCATT TAT
CCCTAGGGA CGGTC CAAGT CAC CGTCA CCAGAC CCTGTCTGAAGTGGGAGTGGTAAATA

240

G I P A R F S G S G S G T D F T L T I Y

BamHI

CCTGTGGAGGCTGATGATGTTGCAACCTATTA CTGTCACCAAAGTAT TGAGGATCCGTAC
GGACACCTCCGACTACTAC AACGTGGATAATGA CAGTGGTTTCATACTCC TAGGCATG

300

CDR 3

P V E A D D V A T Y Y C H Q S I E D P Y
ACGTTCTGAGGGGGGACCAAGCTGGAAATAAAA
TGCAAGCCTCCCCCTGGTTCGACCTTATTTT

333



T F G G G T K L E I K

FIG. 10A

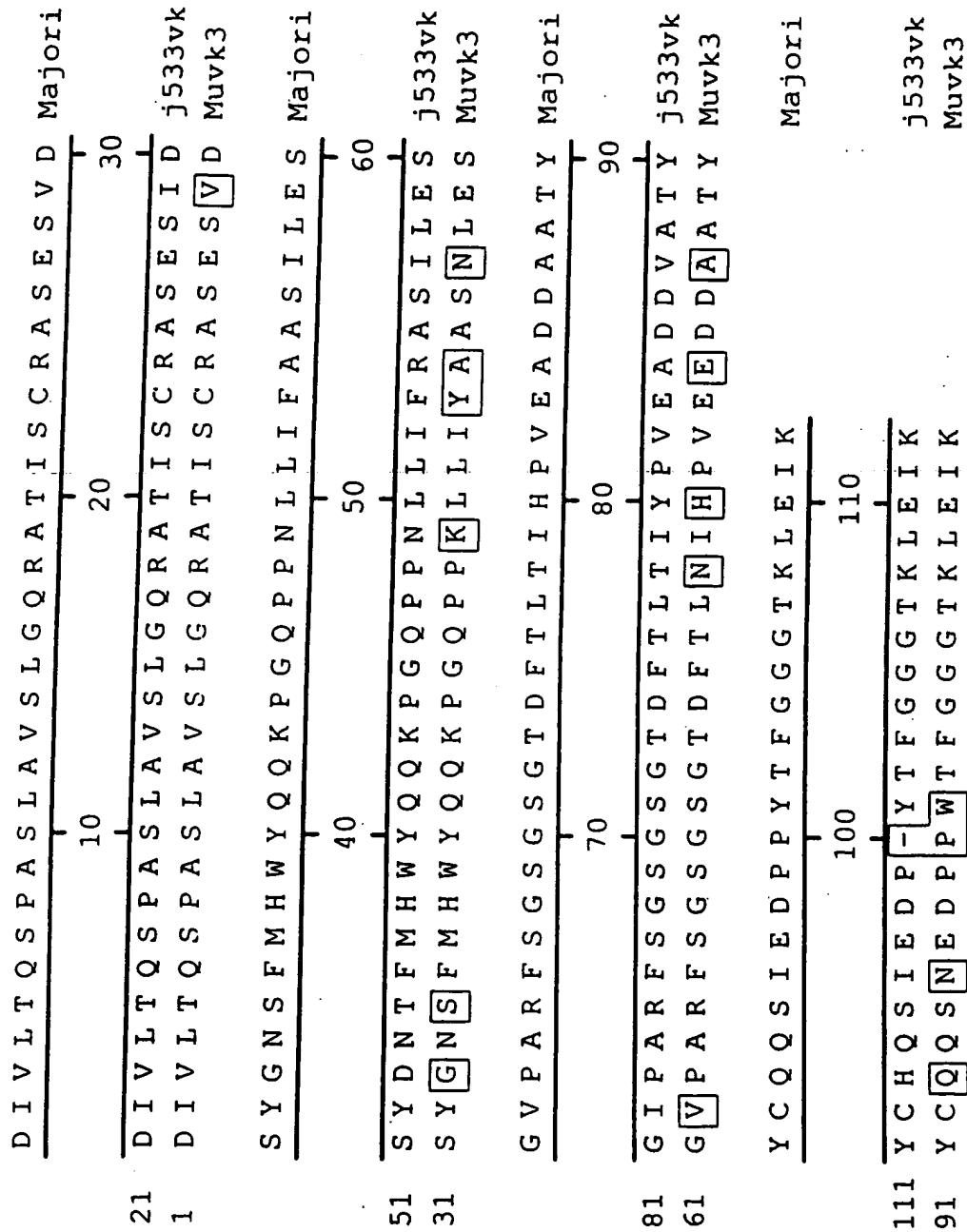


FIG. 10B

Applicant(s): Neil Bander

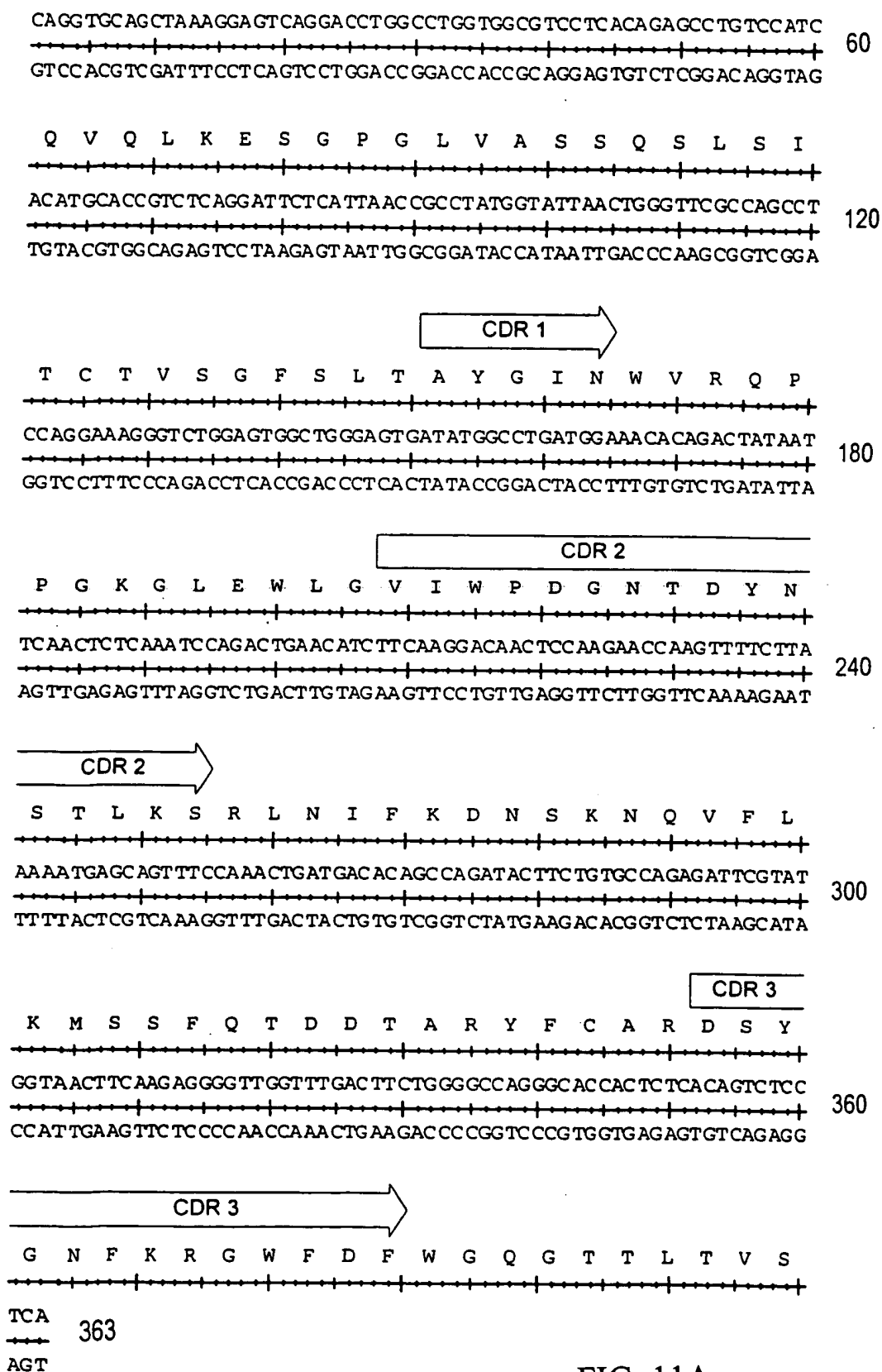
METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
INSULIN-RELATED DISORDERS USING BINDING AGENTS
SPECIFIC FOR PROSTATE SPECIFIC MEMBRANE ANTIGEN

FIG. 11A

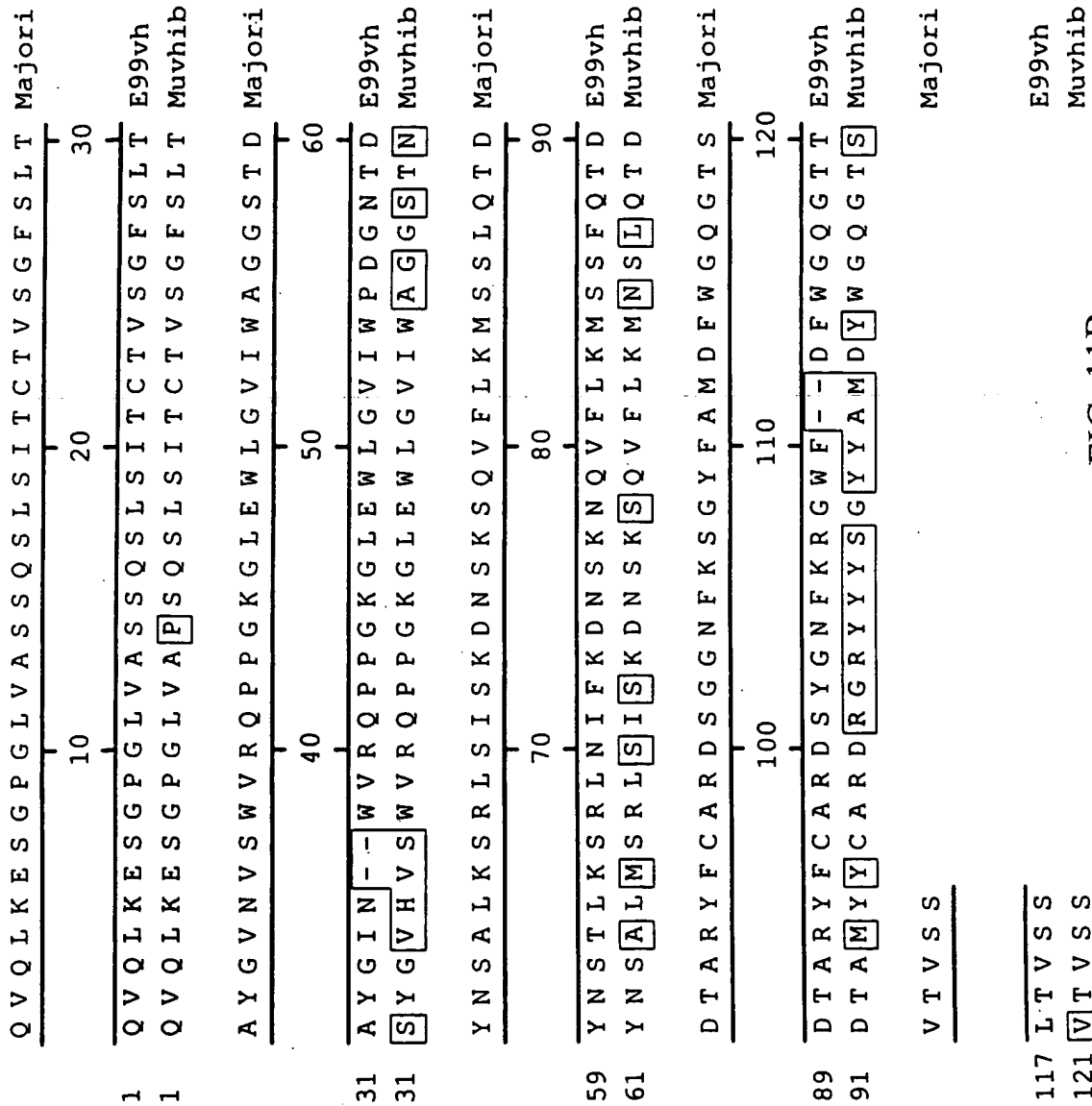


FIG. 11B

Applicant(s): Neil Bander
METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
INSULIN-RELATED DISORDERS USING BINDING AGENTS
SPECIFIC FOR PROSTATE SPECIFIC MEMBRANE ANTIGEN

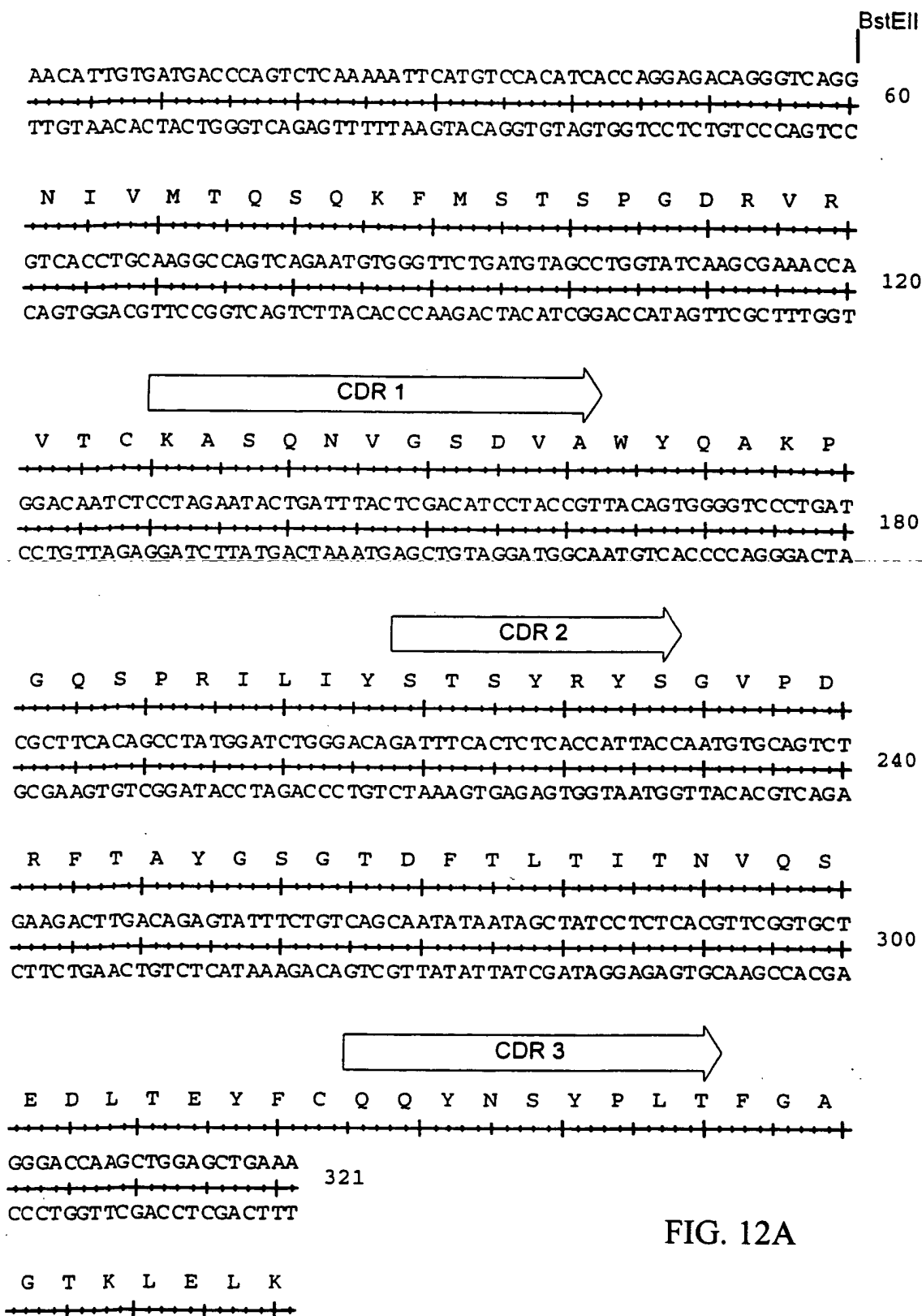


FIG. 12A

METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
INSULIN-RELATED DISORDERS USING BINDING AGENTS
SPECIFIC FOR PROSTATE SPECIFIC MEMBRANE ANTIGEN

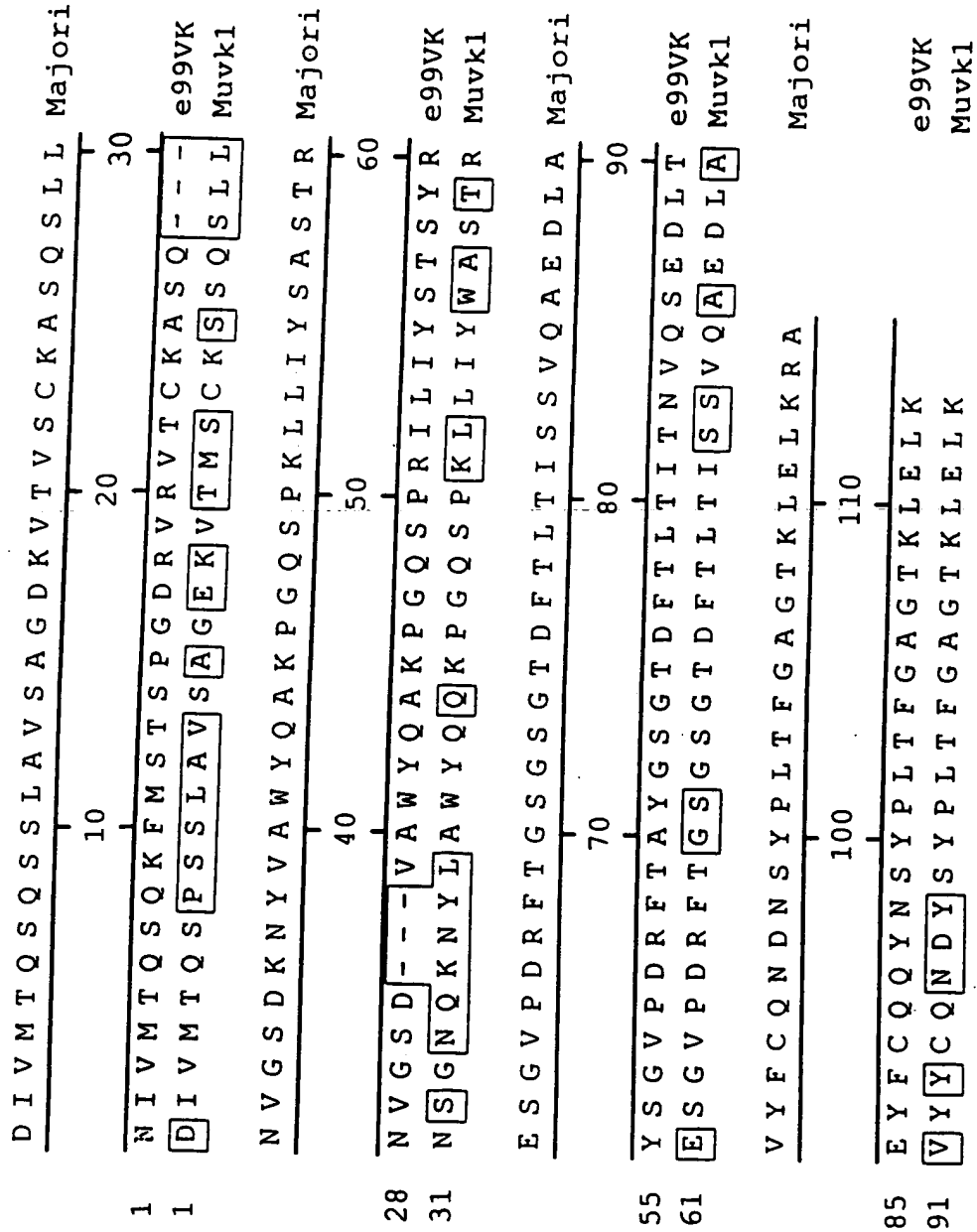


FIG. 12B